

### ***Remarks***

Reconsideration of this Application is respectfully requested.

Claims 6-9 are pending in the application, with claim 6 being the independent claim.

Based on the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding rejections and that they be withdrawn.

#### ***I. Interview Summary***

Applicants would like to thank Examiner Qazi for the courtesy extended during the personal interview with Applicants' representatives, Vince L. Capuano and Lei Zhou on July 16, 2007.

During the interview, the pending rejections under 35 U.S.C. § 103 were discussed. Applicants informed the Examiner that Applicants would consider submitting more data.

#### ***II. Information Disclosure Statement***

Applicants note that a First Supplemental Information Disclosure Statement, citing three (3) copending applications, has been filed on July 18, 2007. Applicants respectfully request the Examiner consider the information disclosed therein.

#### ***III. Rejections under 35 U.S.C. § 103(a)***

The Examiner rejected claims 6-9 under 35 U.S.C. § 103(a) as being unpatentable over Isenring et al. (U.S. Patent No. 6,407,100; "the '100 patent") and Jautelat et al. (U.S. Patent No. 5,789,430; "the '430 patent"). Applicants respectfully traverse this rejection.

Applicants reiterate that for the reasons detailed in Applicants' Reply of May 1, 2006 and Applicants' Reply of October 26, 2006, claims 6-9 are not *prima facie*

obviousness in view of the cited references. In sum, there is nothing in any of the cited patents (including the general statement that active compounds can be combined synergistically), the knowledge in the art, and the nature of the problem to be solved, that would provide a reason for making the specific three-compound combination of trifloxystrobin, prothioconazole, and tebuconazole. Furthermore, even assuming that a *prima facie* case of obviousness is established, the unexpected synergism exhibited by the claimed combination is sufficient to overcome a *prima facie* case.

According to the '100 patent, "combination compositions are suitable for broadening the spectrum of action or for specifically influencing plant growth." Column 8, lines 51-53. According to the '430 patent, known compounds can be combined to, "widen the spectrum of action or to prevent the build up of resistance. In many cases this results in synergistic effects . . ." Column 32, lines 27-29. Taken together, the '100 and '430 patents, at most, teach that compounds can and are often combined. However, none of the cited patents specifically refer to the presently claimed three-compound combination that possesses a synergistic effect.

In contrast to the cited patents, the present invention is directed to a specific combination, which possesses a synergistic effect and comprises trifloxystrobin, prothioconazole and tebuconazole. Neither the combination nor its recited synergistic effect is obvious in view of the cited art.

#### ***IV. Synergistic Effect***

##### ***a. Synergistic Effect***

The Examiner requested Applicants to "explain in detail the synergism." Applicants note:

1. According to the Examiner, synergism means "the combined action of two or more agents . . . that is greater than the sum of the action of one of the agents used alone." Office Action, p. 5, citing *In re Luvisi et al.*, 144 USPQ 646.

2. The data at page 11 in the specification shows that when acting alone at an application rate of 100 g/ha, each individual component of the combination, trifloxystrobin, prothioconazole and tebuconazole has a percent efficacy of 67%, 56% and 22%, respectively. For the reasons detailed in Applicants' Supplemental Reply of January 29, 2007, assuming a linear dose-response correlation, when acting alone at an application rate of 35 g/ha, trifloxystrobin has an expected percent efficacy of 23%; when acting alone at an application rate of 30 g/ha, prothioconazole has an expected percent efficacy of 17%; and when acting alone at an application rate of 35 g/ha, tebuconazole has an expected percent efficacy of 8%. The sum of expected percent efficacy of the three components acting alone at the application rate of 35 g/ha of trifloxystrobin, 30 g/ha of prothioconazole and 35 g/ha of tebuconazole is 48%<sup>1</sup>.

3. The data at page 11 in the specification shows that for the combination, at the application rate of 35 g/ha of trifloxystrobin, 30 g/ha of prothioconazole and 35 g/ha of tebuconazole, the combination has an observed efficacy of 78%, much greater than the expected efficacy of 48% for the three-component combination. Therefore, the claimed combination has a synergistic effect because the combined action of the trifloxystrobin, prothioconazole and tebuconazole is much greater than the sum of the action of trifloxystrobin, prothioconazole and tebuconazole used alone.

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<sup>1</sup> 23% + 17% + 8% = 48%

Alternatively, and in addition to the mathematical calculation of synergistic effect presented above, the synergistic effect of the present invention can be explained as follows:

1. The data at page 11 in the specification shows that when acting alone at an application rate of 100 g/ha, each individual component of the combination, trifloxystrobin, prothioconazole and tebuconazole has a percent efficacy of 67%, 56% and 22%, respectively. Therefore, trifloxystrobin with a 67% efficacy is the most potent fungicide in the combination.
2. While keeping the same application rate of 100 g/ha, but substituting 65 g of the most potent trifloxystrobin (67%) with 30 g of less potent prothioconazole (56%) and 35 g of much less potent tebuconazole (22%), the resulting three-component combination has a percent efficacy of 78%, much greater than that of even the most effective fungicide trifloxystrobin (67%) used alone at 100 g/ha. The improved efficacy can only be the result of a synergistic effect between the three components because in the absence of a synergistic effect, the resulting three-component combination would be expected to have a percent efficacy less than that of trifloxystrobin (67%) used alone. Therefore, the three-component combination of trifloxystrobin, prothioconazole and tebuconazole as claimed has a synergistic effect.

*b. Additional evidence of synergism*

The data at page 11 in the specification shows the synergistic effect of the three-component combination of trifloxystrobin, prothioconazole and tebuconazole at the weight ratio of 1:0.85:1. Additional data of the three-component combination at a

different ratio is provided in the accompanying Declaration by Dr. Peter Dahmen under 37 C.F.R. § 1.132 submitted herewith.

The study described in Table 1 in the Declaration shows the fungicidal effect of a combination of trifloxystrobin, prothioconazole and tebuconazole at the weight ratio of 1:1:1. *Blumeria graminis* fungus on wheat was tested. In this study, the wheat plants were first treated with trifloxystrobin, prothioconazole, tebuconazole or a combination of trifloxystrobin, prothioconazole and tebuconazole. Then, *Blumeria graminis* fungus was introduced to the treated wheat plants to test the preventative (protective) effect of the fungicides. As shown in Table 1, when acting alone at an application rate of 3.3 ppm (parts per million), each individual component of the combination, trifloxystrobin, prothioconazole or tebuconazole has a percent efficacy of 63%, 0% and 11%, respectively. According to Colby formula, the calculated percent efficacy of the combination is 67%. However, the observed percent efficacy is 75%, greater than the calculated percent efficacy. Therefore, the combination of trifloxystrobin, prothioconazole and tebuconazole at the weight ratio of 1:1:1. has a synergistic effect against *Blumeria graminis* fungus on wheat.

The study described in Table 2 in the Declaration shows the fungicidal effect of a combination of trifloxystrobin, prothioconazole and tebuconazole at the weight ratio of 1:1:1. *Fusarium culmorum* fungus on wheat was tested. In this study, the wheat plants were first infested with *Fusarium culmorum* fungus. Then, the infested wheat plants were treated with trifloxystrobin, prothioconazole, tebuconazole or a combination of trifloxystrobin, prothioconazole and tebuconazole to test the curative effect of the fungicides. As shown in Table 2, when acting alone at an application rate of 10 ppm

(parts per million), each individual component of the combination, trifloxystrobin, prothioconazole and tebuconazole has a percent efficacy of 29%, 57% and 57%, respectively. For the reasons detailed in Applicants' Supplemental Reply of January 29, 2007, assuming a linear dose-response correlation, when acting alone at an application rate of 3.33 ppm, trifloxystrobin has an expected percent efficacy of 10%<sup>2</sup>; when acting alone at an application rate of 3.33 ppm, prothioconazole has an expected percent efficacy of 19%<sup>3</sup>; and when acting alone at an application rate of 3.33 ppm, tebuconazole has an expected percent efficacy of 19%<sup>4</sup>. The sum of the expected percent efficacy of the three components acting alone at the application rate of 3.33 ppm of trifloxystrobin, 3.33 ppm of prothioconazole and 3.33 ppm of tebuconazole (total application rate of 10 ppm) is 48%<sup>5</sup>. However, at the application rate of 10 ppm of the combination containing 3.33 ppm of trifloxystrobin, 3.33 ppm of prothioconazole and 3.33 ppm of tebuconazole, the combination has an observed efficacy of 71%, much greater than the sum of expected efficacy of 48% of the three components acting alone at the same application rate. Therefore, the combination of trifloxystrobin, prothioconazole and tebuconazole at the weight ratio of 1:1:1. has a synergistic effect against *Fusarium culmorum* on wheat.

**c. Synergism on other phytopathogenic fungi**

The Examiner stated that the data on page 11, Table A in the specification is *Pyrenophora teres* test on barley and "the synergism as claimed cannot be predicated for the effect on any other phytopathogenic fungi". Office Action, p. 5, under "Claim

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<sup>2</sup> 29% x(3.33/10) = 10%

<sup>3</sup> 57% x(3.33/10) = 19%

<sup>4</sup> 57% x(3.33/10) = 19%

<sup>5</sup> 10% + 19% + 19% = 48%

Rejection - 35 USC § 103" and p. 6, under "Data in Specification and Response to Remarks."

Additional testing of the three-component combination for other phytopathogenic fungi and on other crops is provided in the accompanying Declaration by Dr. Peter Dahmen. The examples disclosed in the Declaration describe *Blumeria graminis* and *Fusarium culmorum* fungi test on wheat. These examples provide further evidence that the claimed combination has synergistic effect in controlling fungi on crops or plants. Therefore, Applicants respectfully submit that the data supports the conclusion that the claimed combination has a synergistic effect in controlling fungi.

*d. Colby formula*

The Examiner questioned the validity of the Colby formula, citing *Ex parte Quadranti*. Office Action, p. 6-7, under "Data in Specification and Response to Remarks." Applicants discussed the Colby formula in the specification to illustrate one method of calculating an expected efficacy of a given three-component combination. However, as shown above, Applicants do not rely solely on the Colby formula to determine an expected efficacy of three-component combination of trifloxystrobin, prothioconazole and tebuconazole. Thus, a showing of synergism does not depend on the validity of Colby formula alone.

*e. In re Lemin et al., 408 F.2d 1045; 161 USPQ 288 (1969)*

The Examiner cited *In re Lemin et al.*, 161 USPQ 288 for the proposition that in order to show synergism, it is necessary to present data "for each component singly at the total rate applied in combination in addition to the fact that each component must be tested individually at the rate at which it appears in combination." Office Action, p. 5,

under "Claim Rejection - 35 USC § 103", and p. 7, "Data in Specification and Response to Remarks".

As discussed above, with regard to the data on page 11 in the specification, Applicants have shown the expected efficacy of individual components at the rate at which it appears in combination are 23%, 17% and 8% for trifloxystrobin, prothioconazole and tebuconazole respectively.

Furthermore, with regard to the data in Table 2 in the Declaration, Applicants have shown the expected efficacy of individual components at the rate at which it appears in combination are 10%, 19% and 19% for trifloxystrobin, prothioconazole and tebuconazole respectively.

For the reasons set forth in Applicants' previous replies, and in view of the arguments presented above, Applicants respectfully submit that the data supports the conclusion that the observed efficacy of the three-component combination of trifloxystrobin, prothioconazole and tebuconazole is greater than that of the sum of expected percent efficacy of the three components acting alone and, therefore, is a synergistic effect. Reconsideration and withdrawal of the outstanding rejection is earnestly solicited.

***Conclusion***

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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